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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,456	10/09/2003	Oscar Johannes Maria Goddijn	46047/MOGUSDIV	9930

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EXAMINER	
PAGE, BRENT T	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/682,456	GODDIJN ET AL.	
	Examiner	Art Unit	
	Brent Page	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5,6,8,21-23,34,36,47,48 and 99-101* is/are pending in the application.

4a) Of the above claim(s) *5,6,8,47,48 and 99-101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,21-23,34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/171,937.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/09/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 5-6, 8, 47-48 and 99-101 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/19/2006.

Claim Objections

Claims 21-23, 34 and 36 are objected to because of the following informalities: The claims use the abbreviations "TPP" and "TPS". The first recitation of each abbreviation should be replaced with the full name of the enzyme, followed by the abbreviation in parentheses. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3, 21-23, 34 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a method for the inhibition of carbon flow in the glycolytic direction in any cell by increasing the intracellular availability of trehalose-6-

phosphate characterized in that the increase is effected by a decrease in TPP activity by transforming the cell with a vector comprising the antisense gene of TPS, a cloning vector comprising any antisense gene for any TPP, and a plant transformed with said vector.

In contrast, the specification only provides guidance for the decrease of TPP activity in plant cells transformed with a vector comprising the full-length antisense gene for TPP of the native plant species. The specification does not provide guidance for the decrease of TPP activity by transforming any other type of cells with any other gene such as TPS or any other organismal TPP other than E. coli or the native plant species.

The function of trehalose phosphate phosphatases is not known in all plant and animal species, and is therefore unpredictable. Vogel et al (The Plant Journal 1998, 13:673-683) disclose the screening and cloning of trehalose phosphate phosphatases from *Arabidopsis thaliana*. Vogel et al state, "While we provide evidence for the occurrence of genes encoding a specific trehalose-6-phosphate phosphatase in plants, it remains to be seen where and when the enzymes, as well as their putative products, are actually present in plant tissues." Vogel et al also state "We also envisage constitutive expression and antisense expression of AtTPPA and AtTPPB in Arabidopsis in order to elucidate further the role of these two novel genes, as well as trehalose metabolism in general, in plants."

In addition to the unpredictability of the function of plant-derived trehalose phosphate phosphatases developmentally, it is also unknown whether plants produce constitutively, or otherwise, amounts of trehalose phosphate synthase that may affect

the expression of trehalose phosphate phosphatase. Vogel et al further state, "Indeed, among the EST of *Aribidopsis* and rice there are homologues of yeast and bacterial trehalose-6-phosphate synthases. However, it still has to be shown that one or more of these homologues is functionally active." Given the unpredictability in the state of the art, it is not known whether plants or any other organims transformed with trehalose phosphate phosphatase genes or antisense constructs from sources other than E. coli would result in the same effect as plants or other organisms transformed with E. coli-derived trehalose phosphate phosphatase genes.

The effect of constitutive promoters on the expression and function of trehalose phosphate biosynthesis genes are unpredictable. Goddijn et al (US Patent 6,833,490) disclose a tobacco plant transformed with a TPP gene under control of the constitutive 35ScaMV promoter. Goddijn et al found that the expression of TPP in all plant parts caused a stunted phenotype in tobacco plants (see column 28, Example 2, for example). Romero et al (Planta, 1997 201:293-297) disclose a tobacco plant transformed with the yeast trehalose-6-phosphate synthase gene. Romero et al found that many deleterious effects were encountered when trehalose accumulated due to the expression of trehalose biosynthesis genes (see page 295 first paragraph). Romero et al state, "A large fraction (40%) of F_0 trehalose-accumulating plants exhibited different degrees of phenotypic change, related to loss of apical dominance, stunted growth, lancet shaped leaves, and some sterility".

Furthermore, the phrase "an antisense-TPP sequence" present in both claim 34 and claim 36 is interpreted by the examiner to include any nucleotide sequence that is

antisense to any part of the TPP sequence which would include nucleotide sequences with identity to as little as two nucleotides of a full-length antisense-TPP sequence. The claims therefore encompass a multitude of DNA molecules.

In contrast, the specification only provides guidance for a DNA molecule in which the entire antisense TPP gene is used as the antisense-TPP sequence, and does not provide guidance for any other DNA sequences as antisense-TPP sequences that would function to restore male fertility under the control of an inducible promoter.

The effect of the expression of antisense molecules on the expression of a corresponding gene and its function is unpredictable. Heuer et al (Plant Physiology 2001 127:33-45) disclose the transformation of maize plants with a *ZmMADS3* antisense construct that encompassed the 3' untranslated portion of the *ZmMADS3* gene, known for its importance in organ development. Heuer et al learned that no phenotypic change was observed in plants carrying and expressing the antisense DNA (see page 37, last paragraph).

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to isolate functional trehalose phosphate phosphatase genes from all sources as claimed. Undue experimentation would have also been required to obtain and evaluate a multitude of antisense fragments for their ability to inhibit TPP gene expression. Undue experimentation would have also been required to obtain viable and morphologically normal plants or other organisms following transformation with a TPP gene under the control of a multitude of non-exemplified promoters. The Federal Courts have

determined that a significant number of inoperative embodiments is deemed to indicate an undue amount of experimentation (see Atlas Powder Co. v. E.I. du Pont de Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

Claims 3, 21-23, 34 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method for the inhibition of carbon flow in the glycolytic direction in any cell by increasing the intracellular availability of trehalose-6-phosphate characterized in that the increase is effected by a decrease in TPP activity by transforming the cell with a vector comprising the antisense gene of TPS, a cloning vector comprising any antisense gene for any TPP, and a plant transformed with said vector.

In contrast, the specification only provides guidance for the decrease of TPP activity in plant cells transformed with a vector comprising the full-length antisense gene for TPP of the native plant species. The specification does not provide guidance for the decrease of TPP activity by transforming any other type of cells with any other gene such as TPS or any other organismal TPP other than E. coli or the native plant species.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed

subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Id.

See also MPEP section 2163, page 174 of chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties".

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the actual method steps that would effect the increase of trehalose-6-phosphate. There are no method steps in claims 3 and 21 that disclose the intended invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 21, 22, 34 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Londesborough et al (US Patent 5422254).

The claims are broadly drawn to a method for the inhibition of carbon flow in the glycolytic direction in any cell by increasing the intracellular availability of trehalose-6-phosphate characterized in that the increase is effected by a decrease in TPP activity, a cloning vector comprising any antisense gene for any TPP, and a plant transformed with said vector.

Londesborough et al teach a crop plant transformed with a cloning vector comprising a yeast TPS gene, wherein the TPS inherently comprises at least one nucleotide that would be in antisense orientation to the TPP gene. The increase in TPS expression resulting in trehalose-6-phosphate accumulation inherently results in feedback inhibition of TPP. Londesborough also teaches the evaluation of a fragment of the TSSL gene that leads to a decrease in TPP activity (see Column 1 lines 10-12, Column 3 line 67, Column 4 Lines 4-5, Column 5 lines 13-25, Examples 7, 8 and 15, for example).

Claims 23 is free of the prior art given the failure of the prior art to teach or reasonably suggest the transformation of a cell with a cloning vector comprising the antisense gene of TPS.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brent Page whose telephone number is (514)-272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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